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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,426	07/02/2001	Kazutoshi Watanabe	P20810	7478

7055 7590 02/06/2003

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EXAMINER
TRUONG, TAMTHOM NGO

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 02/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/787,426	WATANABE ET AL.	
	Examiner	Art Unit	
	Tamthom N. Truong	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *7* is/are allowed.

6)☒ Claim(s) *1-6 and 8-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

It is acknowledged that applicant elects with traverse of species (e), i.e., compounds of formula (I) wherein R^1 is $-N(R^4)-W-R^5$. The traversal is on the ground that the examiner has not given "an appropriate explanation" for a "serious burden" of searching as set forth in MPEP 803. Said traversal is not found persuasive for reasons stated below:

A. Because this is a 371 application, the election of species was done under PCT Rule 13.1, Lack of Unity. Although all species share a special technical feature of (6-pyridyl)-pyrimidin-4-one, said special technical feature does not define a contribution over the prior art, i.e., it can be anticipated by or obvious in view of the prior art.

B. The serious burden of searching arises from the combination of pyridyl, pyrimidinone, and various groups represented by R^1. Moreover, an on-line search on the pyridyl-pyrimidinone alone would yield a large number of hits, which would pose the risk of missing relevant references.

The "Election of Species" is still deemed proper, and is therefore mad FINAL.

Claims 1-12 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 9 appears to claim compounds of formula (I) despite the preamble of "A tau protein kinase 1 inhibitor". Thus, said claim is a substantial duplicate of claim 1 since the preamble does not have patentable weight.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 10-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Said claims recite "the medicament...used for **preventive** [emphasis added]..." They also recite said medicament in the treatment of many diseases that have different etiologies which are not related to "tau protein kinase 1".

The following factors have been considered in the determination of an enabling disclosure:

(1) The quantity of experimentation necessary;

(2) The amount of direction or guidance presented;

(3) The state of the prior art;

(4) The relative skill of those in the art;

(5) The predictability or unpredictability of the art;

(6) The breadth of the claims;

[See ***Ex parte Forman***, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also ***In re Wands***, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

Claims 10-12 recite a medicament used for **"preventive"** therapy for diseases that currently do not even have an effective treatment such as: Alzheimer's, Down syndrome, "parkinsonism", etc. First of all, Alzheimer's is associated with neurodegeneration which in turn depletes acetylcholine. On the other hand, Down syndrome is related to the extra chromosome. Likewise, "parkisonism" has been associated with dopamine. Thus, with etiologies vary as such; a "preventive" medicament for said diseases or related neurodegerative diseases does not have a sound basis in terms of dosages, duration of therapy, etc. Furthermore, the inhibition of "tau protein kinase 1" only "**may** [emphasis added] possibly suppress the neurotoxicity..., and inhibit the nerve cell death..., thereby cease or defer the progress of" Alzheimer's disease. Such a correlation is a mere speculation on the treatment of Alzheimer's disease, and cannot sufficiently guide one skilled in the art in a "preventive" therapy for Alzheimer's disease. Thus, applying the medicament to the prevention or treatment of Down syndrome, and "parkisonism" would require extensive research, if not undue experimentation.

Note, the "how to use" requirements of 35 USC 112 are not met by disclosing only a pharmacological activity of the claimed compounds if one skilled in the art would not be able to use the compounds effectively without undue experimentation. See **In re Diedrich**, 138 USPQ 128.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1, 2, 4-6, and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by the following references:

a. **Skulnick et. al.** (cited on IDS): For example, see Table 1 (on page 1867), compounds # 108-113. Note, in the reference, the variable R_1 should be X, and variable R_2 should be R. The disclosed compounds have anti-inflammatory activity, and thus claim 8 is also anticipated.

b. **Tani et. al.** (cited on IDS): See intermediate of formula I (a tautomer of pyrimidinone) with R as hydrogen. Since the disclosed compound is only an intermediate, claim 8 is not anticipated by Tani et. al.

Compounds disclosed in the above references are embraced by the claimed formula (I) with the following substituents:

i. R^1 is $-N(R^4)-W-R^5$, with W as a single bond; R^4 and R^5 are either hydrogen or $-CH_3$ (or C_1-alkyl);

ii. R^2 is $-CH_3$ (or C_1-alkyl) or halogen;

iii. R^3 is 4-pyridyl (also, 2- or 3-pyridyl).

4. Claims 1, 2, 4, 5, and 8 are rejected under 35 U.S.C. 102(b) as being inherently anticipated by **Stringfellow et. al.** (US 4,619,933), or **Fast et. al.** (US 4,507,302). On column 18, a compound of *2-amino-5-bromo-6-(2-pyridyl)-4-pyrimidinol* [a tautomer of pyrimidinone], which is embraced by the claimed formula I with the following substituents:

iv. R^1 is $-N(R^4)-W-R^5$, with W as a single bond; R^4 and R^5 are hydrogen.

v. R^2 is halogen;

vi. R^3 is 2-pyridyl.

The disclosed compound is used to treat arthritis or aplastic anemia, and thus, the medicament in the instant claim 8 is also anticipated.

5. Claims 1, and 4-6 are rejected under 35 U.S.C. 102(b) as being anticipated by **Brana et. al.** (cited on the IDS). The pyrimidinone derivative of formula I is embraced by the claimed formula I with the following substituents:

vii. R^1 is a substituted aryl;

viii. R^2 is cyano (or CN);

ix. R^3 is 4-pyridyl.

6. Claims 1-6, and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by the following references:

c. **Tani et. al.** (CA 84: 44112b – cited on IDS): The disclosed compound of formula I is a tautomer of a compound of the claimed formula I with the following substituents:

x. R^1 is a heterocyclic group (i.e., morpholino);

xi. R^2 is hydrogen;

xii. R^3 is 2-, 3-, or 4-pyridyl.

d. **Tani et. al.** (JP 49-035631, JP 49-035633, JP 49-035634 (cited on IDS) – also see CAS printout): Tani et. al. disclose pyrimidinone compounds that are embraced by the instant formula I with the following substituents:

xiii. R^1 is $-N(R^4)-W-R^5$, with W as a single bond; R^4 and R^5 are either hydrogen or $-CH_3$ (or C_1-alkyl);

xiv. R^2 is hydrogen;

xv. R^3 is 4-pyridyl (also, 2- or 3-pyridyl).

The disclosed compounds have anti-inflammatory activity, and thus the medicament recited in claim 8 is also embraced.

7. Claims 1, 4, 5, and 8 rejected under 35 U.S.C. 102(b) as being anticipated by **Ram** (Chemical Abstract 116:59167—see the compound in CAS printout). The disclosed compound is embraced by the claimed formula I with the following substituents:

xvi. R^1 is $-N(R^4)-W-R^5$, with W as a single bond, either R^4 or R^5 is hydrogen while the other is a substituted aryl;

xvii. R^2 is cyano (or CN);

xviii. R^3 is 3-pyridyl.

The claimed compound has the antileishmanial activity, and thus the medicament recited in claim 8 is also anticipated.

8. Claims 1, 4, and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by **Buehler et. al.** (CA 65:90645 – also see CAS printout). A pyridinium salt of *1-(2-amino-1,6-dihydro-5-nitro-6-oxo-4-pyrimidinyl)-pyridinium,* which is embraced by the claimed formula I with the following substituents:

xix. R^1 is $-N(R^4)-W-R^5$, with W as a single bond, both R^4 and R^5 are hydrogen;

xx. R^2 is nitro;

xxi. R^3 is 1-pyridyl (note, claims 1, 4, and 5 never specify how the pyridyl ring bonded to the pyrimidinone ring).

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

10. Claims 1, 4-6, and 8 are rejected under 35 U.S.C. 102(e) as being anticipated by **Spohr et. al.** (US 6,096,753). Several compounds listed on column 83 are embraced by the instant formula I with the following substituents:

xxii. R^1 is $-N(R^4)$-W-R^5, with W as a single bond, either R^4 or R^5 is hydrogen while the other is substituted alkyl;

xxiii. R^2 is substituted aryl;

xxiv. R^3 is 4-pyridyl.

11. Claims 1, 4-6, and 8 are rejected under 35 U.S.C. 102(a) as being anticipated by **Spohr et. al.** (WO 98/24780 or WO 98/24782). Several compounds listed on page 124 are embraced by the instant formula I with the following substituents:

xxv. R^1 is $-N(R^4)-W-R^5$, with W as a single bond, either R^4 or R^5 is hydrogen while the other is substituted alkyl;

xxvi. R^2 is substituted aryl;

xxvii. R^3 is 4-pyridyl.

12. Spohr's compounds are used to treat inflammation, pain and diabetes, and thus, the medicament recited in claim 8 is also anticipated.

Allowable Subject Matter

Claim 7 is allowable since the references of record do not disclose species recited in claim 7.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 703-305-4485. The examiner can normally be reached on M-F (9:00-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 703-308-4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

T. Truong
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February 4, 2003

RICHARD L. RAYMOND
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